Claim 29, line 1, delete "being" and replace it with--comprising--, and lines 1-2, delete "having the characteristics of" and replace it with--comprising chemistry similar to--.

Claim 30 (once amended) [An effective therapeutic dosage of] A deproteinated urine or serum of a fasting bear which has not eaten for two weeks or more comprising a therapeutic compound producing, in any combination, the following behavior in another mammal: tranquility, reduced heart rate, increased osteoblastic activity, or decreased osteoclastic activity.

Claim 44, line 2, delete "active" and line 3, delete "active".

Claim 45, line 3, delete "active" and line 4, delete "active".

Claim 64, line 1, delete "taken from" and replace it with--comprising--.

REMARKS

Reexamination of the application as amended is respectfully requested.

A. PRIORITY (35 USC §120)

1. Original application serial number 08/079,089, filed June 16, 1993 entitled "Denning Bear Isolate and Method" is still pending.

2. Continuation in part application serial number 08/259,788, filed June 14, 1994 and entitled "Denning Bear Isolate and Method" is still pending.

3. Continuation in part application serial number 08/470,750 filed June 6, 1995 and entitled "Fasting Bear Isolate and Method" is still pending.

B. CLAIMS REJECTION (35 USC §112, FIRST PARAGRAPH)

1. The Examiner rejected claims 63-65 under 35 USC §112, first paragraph, arguing that the specification does not reasonably provide enablement for a pharmacological composition comprising 24,25-dihydroxyvitamin D3 (D3) or a composition having a molecular weight of one

hundred or less. The Examiner further argues that the specification does not provide for predictable evidence that the D3 or a composition having a molecular weight of one hundred or less are the active ingredients responsible for the bone formation. Applicants respectfully disagree. On page 28, beginning on line 8, there is a discussion of the activity of D3. Specifically, it is noted that 1,25-dihydroxyvitamin D3 (1,25) unopposed produces bone loss, high blood calcium, and death. It is noted that to prevent this occurrance, a denning bear reduces production of 1,25 and increases production of D3. The inventors further note that historically D3 has been thought to have no metabolic action, but in fact, the inventors have found that it actually stimulates bone deposition. The increase in the ratio of D3 to 1,25 prevents 1,25 from releasing calcium from bone and causes the D3 to recycle calcium back into bone.

Beginning on page 46, line 29, and continuing through page 55, line 11, there is a discussion of the bone remodeling capabilities of Bear Drived Isolate (BDI). It is also shown on page 27, beginning at line 20 through page 28, line 26, that BDI contains D3. Without BDI, and hence D3, ovariectomized mice and guinea pigs show marked bone loss. Those same mice and guinea pigs administered BDI, and again D3, show marked bone remodeling.

Thus, it is Applicants' position that their specification does support a patentable claim identifying D3 as an active substance which stimulates bone formation. Applicants respectfully request, therefore, that Examiner withdraw her rejection to claims 63 and 65. Applicants have canceled claim 64.

C. CLAIMS REJECTION (35 USC §112, SECOND PARAGRAPH)

The Examiner rejected 1-21, 24-30, 44-45, and 63-66 under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants have amended the appropriate

above identified Claims to delete the phrase "having the characteristics" and replacing it with--chemistry similar to--. Applicants believe that the amendment more clearly identifies the compositions claimed as having a chemical structure like that of the blood or urine of a fasting bear. Applicants submit that the amendment removes the vagueness of the claims and more particularly points out and distinctly claims the subject matter which Applicants regard as the invention.

Similarly, Applicants amended Claim 17 to delete reference to a Bear Drived Isolate and replace it with an isolate. Applicants believe that this amendment more clearly identifies an isolate which later in the Claim is identified as being from the urine or serum of a fasting bear. Thus, Applicants submit that this amendment more particularly points out and distinctly claims the subject matter which Applicants regard as the invention.

Applicants have adopteed the Examiner's suggestion in claims 12-15 and the term "substance" has been deleted and replaced with the term "compound".

In Claim 13, Applicants amended the claim to add the word "marker" in the phrase "signature marker exhibited in the deep proteinated isolate of urine or blood". Applicants submit that the key to Claim 13 is a deproteinated isolate which exhibits an ability to cause tranquility, reduction in body temperature, or heart rate. The compound must include the signature BDI in order to produce such effects. Thus, the isolate does have a "signature" which can be identified as BDI ("the marker").

Claims 1-15 and 18 have been amended to include transitional language which defines more particularly what the composition is as opposed to what it does from a functional standpoint.

Finally, in Claims 44 and 45, Applicants have deleted the term "active" from the phrase

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"active substance". Applicants believe that this amendment more particularly points and distinctly claims the subject matter which they regard as the invention inasmuch as the compound extracted from the urine or serum of a fasting bear, whether active or inactive, acts as an inhibitor of osteoblastic activity.

D. Double Pattenting (35 USC §101)

The Examiner rejected Claims 32 and 33 arguing that they are substantially duplicative of claim 31. Applicants respectfully disagree. Claim 31 is directed to a multitude of effects in *guinea pigs* injected with a composition of matter comprising the deproteinated urine or serum of a fasting bear. Claim 32, however is directed only to enhance the bone remodeling, which is not claimed in Claim 31, in guinea pigs injected with the composition. Applicants submit that if the composition of matter of Claim 31 is administered, either increased osteoblastic activity, decreased osteoclastic activity, or a combination of both may occur. Increased osteoblastic activity with corresponding increased osteoclastic activity may not result in enhanced bone remodeling. Likewise, decreased osteoclastic activity without increased osteoblastic activity will not result in enhanced bone remodeling. Finally, a combination of increased osteoblastic activity and decreased osteoclastic activity may result in enhanced bone remodeling only if the original levels were normal to begin with.

Applicants further submit that the claim 33 is directed to an ovariectomized rat in which administration of the composition of matter causes enhanced bone formation. As evidenced by the Specification examples, guinea pigs and rats reacted differently, albeit positively, to administration of the composition of matter. Applicants respectfully submit, therefore, that claims 32 and 33 are properly drawn claims and request that the Examiner withdraw her rejection to these two claims.

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The Examiner also rejected claim 49 on double patent on grounds arguing that it is duplicative of claim 48. Again, Applicants respectfully disagree. Claim 48 is directed to a composition of matter obtained from a *fasting* black bear which has not eaten for *two weeks or more*. Claim 49, on the other hand, is directed to a *denning* black bear which neither eats, drinks, urinates, or defecates for lengthy periods of time. Applicants submit that a fasting bear may drink, urinate, and defecate. Further, the "lengthy period of time" identified in claim 49 can exceed the two week limitation of claim 48. Applicants respectfully submit, therefore that claim 49 contains distinctly subject matter from claim 48 and requests that the Examiner withdraw her rejection on this ground.

Finally, the Examiner rejected claim 50 under double patenting grounds arguing that it is duplicative of claim 51. Again, Applicants respectfully disagree. Both Claims 50 and 51 are dependent claims of independent claim 49. Claim 50 is directed to a composition of matter objected to "in vitro" analysis while claim 51 is a composition of matter subjected to "in vivo analysis with ovariectomized rats". Applicants first submit that there is a significant distinction between in vitro and in vivo analysis. Applicants further submit that the in vivo analysis with ovariectomized rats does not show the increased fibroblastic activity of the in vitro analysis of claim 50. Applicants submit, therefore, that claim 51 contains patentable subject matter distinct from that of claim 50 and respectfully request that the Examiner withdraw her rejection on this ground.

For the foregoing reasons, Applicants submit that by the foregoing amendments, those claims rejected under 35 USC §112, second paragraph, are now in order for allowance and respectfully request the Examiner to take such action. Applicants further submit that claims rejected under 35 USC §112, first paragraph, and 35 USC §101 are properly drawn to patentable

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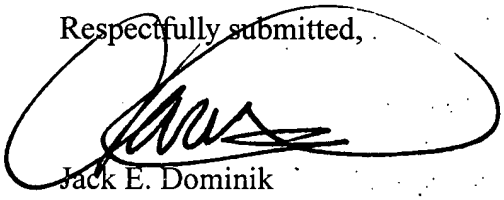
subject matter and respectfully request that the examining attorney issue a Notice of Allowance on those claims.

Should the Examiner believe that an interview with Applicants would be a benefit to move this case forward, please do not hesitate to contact the undersigned.

Respectfully submitted,



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